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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,871	05/09/2001	C. Frank Bennett	ISPH-0543	4942

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,871	BENNETT ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford, Ph.D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/04/04 has been entered.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application; the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 USC § 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The specification in the earlier filed application 09/326,186 did not set forth Example 21 demonstrating the topical administration of antisense targeting B7-1 and B7-2 in a mouse psoriasis model. This example is considered to provide enablement for the instantly claimed invention. In regards to the topical administration of antisense the specification of earlier filed application 09/326,186 was not considered enabling. Therefore Applicant is afforded the filing date of the instant application, 5/09/01.

Response to Arguments

Claim Rejections - 35 USC § 112

3. Claims 1-12 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (New Matter).

Applicants have amended the instant claims to incorporate Genbank Accession No. M27533 (human B7-1) and Genbank Accession No. L25259 (human B7-2) in an effort to properly describe the claimed invention. However, it is noted that the nucleotide sequences corresponding to these GenBank Accession numbers are not set forth in the specification as filed, moreover it is noted that these sequences have been modified several times (see attachment describing the revision history of these sequences), and it is unclear which sequence Applicants actually intended to incorporate as of the filing of the instant specification. Since these sequences were not a part of the original disclosure, this current amendment to the claims is considered new matter. Applicants must amend the claims and remove the new matter in response to this Office Action.

Moreover, the attempt to incorporate subject matter into this application by reference to the human B7-1 and B7-2 DNA sequences set forth in the non-patent publications of GenBank Accession Nos L25259 and M27533, is improper because these DNA sequences are required to properly describe the claimed invention, and are considered essential material. The incorporation of essential material in the specification by reference to a foreign application or

patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stinchcomb et al. (US Pat. No. 5,877,021) or Freeman et al. (US Pat. No. 5,942,607), either in view of Abramowicz et al. (WO 94/17773), and Cooper et al. (WO 93/24134 A1) and further in view of Brand et al.

4. The invention of Stinchcomb et al. features the use of one or more nucleic acid-based techniques e.g. "enzymatic nucleic acid molecules (ribozymes), antisense nucleic acids, 2-5A antisense chimeras, triplex DNA, antisense nucleic acids containing RNA cleaving chemical groups," to induce graft tolerance, to treat autoimmune diseases and to treat allergies by inhibiting the synthesis of B7-1, B7-2, B7-3, CD4O proteins, and other potential targets including ICAM-I (see col. 5, line 66 through col. 6, line 6). In one specific embodiment autoimmune diseases include, for example, psoriasis." (see col. 5, lines 15-20). Stinchcomb et al. further teach that the nucleic acid inhibitors of B7-1 or B7-2 may be delivered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres.

Administration of the ribozyme compositions may include, for example, local, topical, systemic, ocular, intraperiotoneal, oral, and aerosol inhalation (col. 12, lines 18-36)

Freeman et al. teach the use of antisense oligonucleotides complementary to the B7-1 and B7-2 transcripts as a means of blocking B7-l or B7-2 expression in B-lymphocytes. Freeman et al. disclose two specific oligonucleotides, each 17 nucleotides in length, for use as antisense inhibitors of B7-l and B7-2 expression (col. 18, lines 34-5%. Freeman et al. teach the use of antisense compounds to inhibit B7-1 and B7-2 expression by delivering them to cells for the purpose of blocking T cell activation, which should be useful in treating autoimmune diseases (col. 17, line 62 to col. 1 8, line 23).

Stinchcomb et al. and Freeman et al. do not teach antisense oligonucleotides of 8 to 30 nucleobases in length targeting human B7-1 and B7-2, comprising a modified covalent linkage, nucleobase, sugar moiety, or modified with a lipophilic moiety. Additionally, these references do not specifically teach and the use of these antisense compounds in a method for treating, contact dermatitis, atopic dermatitis, seborrheic dermatitis, nummular dermatitis, generalized exfoliative dermatitis or eczema.

Abramowicz et al. teach that interleukin-l (IL-l 0) functions to block the expression of B7 and ICAM-I on human monocytes (page l 1, lines 8-1 1). Abramowicz et al. also teach the use of lL-10 to treat or prevent diseases or conditions associated with the activity of B7 and it's receptor C1728 (see page 12, lines 7-10). In one particular embodiment, Abramowicz teach the use of IL-10 (a B7 and ICAM-1 inhibitor) for the treatment or prevention of diseases selected from inter alia) atopic dermatitis, and chronic eczema (see page 56, lines 22-24).

Cooper et al. teach the use of oligomeric compounds for the treatment of diseases associated with cellular hyperproliferation. These diseases include, for example, psoriasis, chronic dermatitis, psoriasiform dermatitis, and atopic dermatitis (page 20, lines 8-12). The oligomeric compounds of Cooper et al. are preferably 8 to about 40 nucleosidyl units (page 9, lines 26-29). These oligomeric compounds have internucleosidyl linkages linking the nucleoside monomers .and, thus, includes oligonucleotides, nonionic oligonucleoside alkyl- and arylphosphonate analogs, alkyl- and aryl-phosphonothioates, phosphorothioates or phosphorodithioate analogs of oligonucleotides, phosphoramidate analogs of oligonucleotides. The oligomeric compounds also include nucleoside/non-nucleoside polymers wherein the base, the sugar and the phosphorous moiety have been replaced or modified (pages 5-6). In addition, the oligomers of Cooper et al. may comprise conjugation partners such as intercalators, and lipophilic agents, which may further enhance the uptake of the oligomer, modify the interaction of the oligomer with the target sequence, or alter the pharmacokinetic distribution of the oligomer (page 6, line35 to page 7, line 5). Moreover, Cooper et al. teach that oligomers that comprise substituents such as 2'-o-methylribose groups, various base modifications, and analogs of the phosphorous backbone, such as phosphorothioates, can increase resistance to nucleases (page 14, lines 24-27).

[It is noted that in the arguments filed 12-08-03, page 14, Applicants argued that "none of the above cited references provide any working examples of topical in vivo administration of any antisense molecule resulting in a therapeutic benefit."] However, as noted below the prior art at the time of the instant specification provided sufficient guidance for the topical administration of antisense compounds to the skin of an individual.

Brand et al. teach the transdermal delivery of antisense compounds comprising backbone, nucleobases, and sugar modifications (see pages 53-54). In particular Brand et al. provide sufficient guidance and instruction that would allow the skilled artisan to deliver antisense compounds to the skin without undue experimentation.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the teachings of Stinchcomb et al. and Freeman et al. to make the instantly claimed invention, wherein said invention comprises a method for treating inflammatory skin disorders such as dermatitis and eczema, and wherein the method comprises topically applying an antisense compound 8 to 30 nucleobases in length comprising the base, sugar, covalent linkage, and lipophilic modifications taught by Cooper et al. One of ordinary skill in the art would have been motivated to modify the antisense oligonucleotides of Freeman et al. (or the antisense nucleic acid of Stinchcomb et al.) with the sugar, base, the internucleosidyl backbone modifications, and lipophilic agents of Cooper et al. since these modifications are disclosed as enhancing the cellular properties of oligomeric compounds comprising these modifications. Furthermore, the disclosure of Cooper et al. also provides motivation and an expectation of success for the use of modified antisense oligonucleotides of 8 to 40 nucleotides in length for the treatment of various inflammatory skin disorders including dermatitis and psoriasis.

One of ordinary skill in the art would have been motivated to modify the methods of Stinchcomb et al. and Freeman et al. to comprise the treatment of conditions such as atopic dermatitis, and eczema since the prior art (Abramowicz et al.) discloses that these conditions can be treated by administration of an inhibitor of B7 expression.

Furthermore, the ordinary skilled artisan would have been motivated to following the teachings of Brand et al. to deliver antisense compounds to the skin of individuals in need thereof, since this reference provides a non-invasive, simple, and convenient method of delivering antisense compounds to the skin.

Therefore, the invention as a whole would have been prima facie obvious over Stinchcomb et al. or Freeman et al., in view of Abramowicz et al. and Cooper et al. and further in view of Brand et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford, Ph.D. whose telephone number is 571-272-0757. The examiner can normally be reached on Monday-Saturday, Flex Schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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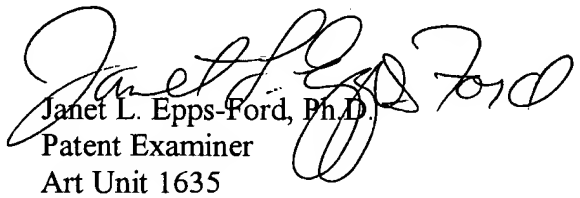

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Patent Examiner
Art Unit 1635

JLE